

CLAIMS

WHAT IS CLAIMED IS:

- 1.) An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:
 - (a) a polynucleotide fragment of SEQ ID NO:1 or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No: PTA-2766, which is hybridizable to SEQ ID NO:1;
 - (b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:2 or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No: PTA-2766, which is hybridizable to SEQ ID NO:1;
 - (c) a polynucleotide encoding a polypeptide domain of SEQ ID NO:2 or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No: PTA-2766, which is hybridizable to SEQ ID NO:1;
 - (d) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:2 or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No: PTA-2766, which is hybridizable to SEQ ID NO:1;
 - (e) a polynucleotide encoding a polypeptide of SEQ ID NO:2 or the cDNA sequence included in ATCC Deposit No: PTA-2766, which is hybridizable to SEQ ID NO:1, having leucine-rich repeat protein activity;
 - (f) a polynucleotide which is a variant of SEQ ID NO:1;
 - (g) a polynucleotide which is an allelic variant of SEQ ID NO:1;
 - (h) an isolated polynucleotide comprising nucleotides 552 to 2450 of SEQ ID NO:1, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 626 of SEQ ID NO:2 minus the start codon;
 - (i) an isolated polynucleotide comprising nucleotides 549 to 2450 of SEQ ID NO:1, wherein said nucleotides encode a polypeptide corresponding to amino acids 1 to 626 of SEQ ID NO:2 including the start codon;
 - (j) a polynucleotide which represents the complementary sequence (antisense) of SEQ ID NO:1;

- (k) a polynucleotide fragment of SEQ ID NO:34 or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No: XXXXX, which is hybridizable to SEQ ID NO1;
- 5 (l) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:35 or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No: XXXXX, which is hybridizable to SEQ ID NO:34;
- (m) a polynucleotide encoding a polypeptide domain of SEQ ID NO:35 or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No: XXXXX, which is hybridizable to SEQ ID NO:34;
- 10 (n) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:35 or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No: XXXXX, which is hybridizable to SEQ ID NO:34;
- (o) a polynucleotide encoding a polypeptide of SEQ ID NO:35 or the cDNA sequence included in ATCC Deposit No: XXXXX, which is hybridizable to SEQ ID NO:34, having leucine-rich repeat protein activity;
- 15 (p) a polynucleotide which is a variant of SEQ ID NO:34;
- (q) a polynucleotide which is an allelic variant of SEQ ID NO:34;
- (r) an isolated polynucleotide comprising nucleotides 565 to 2700 of SEQ ID NO:34, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 626 of SEQ ID NO:35 minus the start codon;
- 20 (s) an isolated polynucleotide comprising nucleotides 562 to 2700 of SEQ ID NO:34, wherein said nucleotides encode a polypeptide corresponding to amino acids 1 to 713 of SEQ ID NO:35 including the start codon;
- (t) a polynucleotide which represents the complimentary sequence (antisense) of SEQ ID NO:35; and
- 25 (u) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(t), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.
- 30 2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a human leucine-rich repeat protein.

3. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.
4. A recombinant host cell comprising the vector sequences of claim 3.
5. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:
 - (a) a polypeptide fragment of SEQ ID NO:2 or the encoded sequence included in ATCC Deposit No: PTA-2766;
 - (b) a polypeptide fragment of SEQ ID NO:2 or the encoded sequence included in ATCC Deposit No: PTA-2766, having leucine-rich repeat protein activity;
 - (c) a polypeptide domain of SEQ ID NO:2 or the encoded sequence included in ATCC Deposit No: PTA-2766;
 - (d) a polypeptide epitope of SEQ ID NO:2 or the encoded sequence included in ATCC Deposit No: PTA-2766;
 - (e) a full length protein of SEQ ID NO:2 or the encoded sequence included in ATCC Deposit No: PTA-2766;
 - (f) a variant of SEQ ID NO:2;
 - (g) an allelic variant of SEQ ID NO:2;
 - (h) a species homologue of SEQ ID NO:2;
 - (i) a polypeptide comprising amino acids 2 to 449 of SEQ ID NO:2, wherein said amino acids 2 to 449 comprise a polypeptide of SEQ ID NO:2 minus the start methionine;
 - (j) a polypeptide comprising amino acids 1 to 449 of SEQ ID NO:2;
 - (k) a polypeptide encoded by the cDNA contained in ATCC Deposit No. PTA-2766;
 - (l) a polypeptide fragment of SEQ ID NO:35 or the encoded sequence included in ATCC Deposit No: XXXXX;
 - (m) a polypeptide fragment of SEQ ID NO:35 or the encoded sequence included in ATCC Deposit No: XXXXX, having leucine-rich repeat protein activity;
 - (n) a polypeptide domain of SEQ ID NO:35 or the encoded sequence included in ATCC Deposit No: XXXXX;

- (o) a polypeptide epitope of SEQ ID NO:35 or the encoded sequence included in ATCC Deposit No: XXXXX;
- (p) a full length protein of SEQ ID NO:35 or the encoded sequence included in ATCC Deposit No: XXXXX;
- 5 (q) a variant of SEQ ID NO:35;
- (r) an allelic variant of SEQ ID NO:35;
- (s) a species homologue of SEQ ID NO:35;
- (t) a polypeptide comprising amino acids 2 to 713 of SEQ ID NO:35, wherein said amino acids 2 to 713 comprise a polypeptide of SEQ ID NO:35 minus
- 10 the start methionine;
- (u) a polypeptide comprising amino acids 1 to 713 of SEQ ID NO:35; and
- (v) a polypeptide encoded by the cDNA contained in ATCC Deposit No. XXXXX.
6. The isolated polypeptide of claim 5, wherein the full length protein
- 15 comprises sequential amino acid deletions from either the C-terminus or the N-terminus.
7. An isolated antibody that binds specifically to the isolated polypeptide of claim 5.
8. A recombinant host cell that expresses the isolated polypeptide of
- 20 claim 15
9. A method of making an isolated polypeptide comprising:
- (a) culturing the recombinant host cell of claim 8 under conditions such that said polypeptide is expressed; and
- (b) recovering said polypeptide.
- 25 10. The polypeptide produced by claim 9.
11. A method for preventing, treating, or ameliorating a medical condition, comprising the step of administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 5 or the polynucleotide of claim 1.
12. A method of diagnosing a pathological condition or a susceptibility to
- 30 a pathological condition in a subject comprising:
- (a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.

13. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

5 (a) determining the presence or amount of expression of the polypeptide of claim 5 in a biological sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

14. A process for making polynucleotide sequences encoding a gene
10 product having altered leucine-rich repeat protein activity comprising,

a) shuffling a nucleotide sequence of claim 1,

b) expressing the resulting shuffled nucleotide sequences and,

15 c) selecting for altered leucine-rich repeat protein activity as compared to the leucine-rich repeat protein activity of the gene product of said unmodified nucleotide sequence.

15. A shuffled polynucleotide sequence produced from the process of claim 14.

16. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence selected from the group consisting of:

20 (a) a polynucleotide encoding a polypeptide of SEQ ID NO:2;

(b) an isolated polynucleotide comprising nucleotides 552 to 2450 of SEQ ID NO:1, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 626 of SEQ ID NO:2 minus the start codon;

25 (c) an isolated polynucleotide comprising nucleotides 549 to 2450 of SEQ ID NO:1, wherein said nucleotides encode a polypeptide corresponding to amino acids 1 to 626 of SEQ ID NO:2 including the start codon;

(d) a polynucleotide encoding the HLRRNS1 polypeptide encoded by the cDNA clone contained in ATCC Deposit No. PTA-2766;

30 (e) a polynucleotide which represents the complimentary sequence (antisense) of SEQ ID NO:1;

(f) a polynucleotide encoding a polypeptide of SEQ ID NO:35;

(g) an isolated polynucleotide comprising nucleotides 565 to 2700 of SEQ ID NO:34, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 713 of SEQ ID NO:35 minus the start codon;

(h) an isolated polynucleotide comprising nucleotides 562 to 2450 of SEQ ID NO:34, wherein said nucleotides encode a polypeptide corresponding to amino acids 1 to 626 of SEQ ID NO:35 including the start codon;

(i) a polynucleotide encoding the HLRRNS1 polypeptide encoded by the cDNA clone contained in ATCC Deposit No. XXXXX; and

(j) a polynucleotide which represents the complimentary sequence (antisense) of SEQ ID NO:35.

17. The isolated nucleic acid molecule of claim 16, wherein the polynucleotide comprises a nucleotide sequence encoding a human leucine-rich repeat protein.

18. A recombinant vector comprising the isolated nucleic acid molecule of claim 16.

19. A recombinant host cell comprising the recombinant vector of claim 18.

20. An isolated polypeptide consisting of an amino acid sequence selected from the group consisting of:

(a) a polypeptide fragment of SEQ ID NO:2 having leucine-rich repeat protein activity;

(b) a polypeptide domain of SEQ ID NO:2 having leucine-rich repeat protein activity;

(c) a full length protein of SEQ ID NO:2;

(d) a polypeptide corresponding to amino acids 2 to 449 of SEQ ID NO:2, wherein said amino acids 2 to 449 comprise a polypeptide of SEQ ID NO:2 minus the start methionine;

(e) a polypeptide corresponding to amino acids 1 to 449 of SEQ ID NO:2;

(f) a polypeptide encoded by the cDNA contained in ATCC Deposit No. PTA-2766;

(g) a polypeptide fragment of SEQ ID NO:35 having leucine-rich repeat protein activity;

- (h) a polypeptide domain of SEQ ID NO:35 having leucine-rich repeat protein activity;
 - (i) a full length protein of SEQ ID NO:35;
 - (j) a polypeptide corresponding to amino acids 2 to 713 of SEQ ID NO:35, wherein said amino acids 2 to 713 comprise a polypeptide of SEQ ID NO:35 minus the start methionine;
 - (k) a polypeptide corresponding to amino acids 1 to 713 of SEQ ID NO:35; and
 - (l) a polypeptide encoded by the cDNA contained in ATCC Deposit No. XXXX.
21. The method for preventing, treating, or ameliorating a medical condition of claim 11, wherein the medical condition is a proliferative disorder.
22. The method for preventing, treating, or ameliorating a medical condition of claim 11, wherein the medical condition is a neural disorder.
23. The method for preventing, treating, or ameliorating a medical condition of claim 11, wherein the medical condition is disorder related to aberrant apoptosis modulation, either directly or indirectly.